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10/670,507	09/26/2003	Jonathan A. Ellman	045413-0114	8613

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,507	ELLMAN ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *3,6-8,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,9-13 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on September 24, 2004.

Status of the Claims

2. Claims 1-18 were pending in the present application.

3. Applicant's *specifically* elected species (Subgroup 4 = ELISA, see attached Interview Summary; Subgroup 5 = Applicants elect a disulfide linking group) were found in the art. Furthermore, Applicant's *specifically* elected species (Subgroup 1 = CD4, Subgroup 2 = 252 member library of disulfide compound having core structure CTBF-S-S-R8 wherein R8 is straight chain alkyl of 1 to 10 carbon atoms substituted with amino and the CTBF-S-S-R8 has less that 500 Daltons, Subgroup 3 = 6-boromo chromone without the aldehyde linking group) were searched and were not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-

type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

4. Claims 3, 6-8 and 14-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in the 9/24/04 response (see below i.e., ***Response to Restriction and/or Election of Species***). Please note that Applicants' statement, "in total, claims 1-3, 6, 7 and 9-18 read on all of the elects subgroups" (see 9/24/04 Response, page 2, last sentence) appears to be in error because claims 14-15 do not read on Subgroup 1 (see 9/24/04 Response, page 2, line 4). In addition, the Examiner notes that Applicants' subgroup 4 species election has been changed from "quantitative spectroscopic property" to "ELISA" (see attached interview summary) and, as a result, claims 3, 6 and 7 also do not read on the claimed invention (claim 8 also does not read on the elected species, see 9/24/04 Response, page 2, last line).

5. Therefore, claims 1-2, 4-5, 9-13, 16-18 are examined on the merits in this action.

Response to Restriction and/or Election of Species

6. Applicant's election of species in the 9/24/04 Response ***with traverse*** is acknowledged.

7. The election of species traversal is on the ground(s) that "there is no undue burden to search of all the subject matter of the claims" (e.g., se 9/24/04 Response, page 2, lines 1-2).

8. These arguments were fully considered but were not found persuasive. The Examiner's position is that the species are distinct, each from the other, because the structures and modes of action of each of the species encompassed are different. They would also differ in their reactivity and/or mechanism and/or the products made. For example, the species of target biological molecule (TBM) have different structures and functions and, as a result, are separately classified (e.g., TBM = enzyme in class 435, subclass 183+; TBM = hormone in class 530, subclass 397; TBM = antibody in class 530, subclass 387.1+, etc.). Likewise, the library of small organic molecules can also be separately classified into hundreds of different class and subclasses depending on the structure of the library members and/or their function (e.g., Library = for peptide in class 435, DIG 35; peptide-nucleic acid in class 435, DIG 36, etc.). The species of candidate target biological fragments, Subgroup 3, and linking group, subgroup 5, could be classified into hundred of different classes and subclasses depending their structure (e.g., classes 532-570 drawn to various organic molecules). Finally, the species of detection can also be separately classified (e.g., Subgroup 4 = NMR is in class 436, subclass 173, Subgroup 4 = X-ray crystallography is in class 378, subclass 73, etc.). Thus, the different species would require different searches and there is no expectation that the searches would be coextensive. Therefore this do create an undue search burden.

9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The information disclosure statement filed September 26, 2003, fails, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because two publications cited therein, numbered A19 and A22, lack publication dates, a necessary element for consideration. While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, these three publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1).

The other references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-2, 9-13, 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Verdine (WO 93/141087) (Date of Patent is **July 22, 1993**).

For ***claim 1***, Verdine (see entire document) discloses methods for designing and producing sequence-specific DNA binding proteins (e.g., see Verdine, abstract), which anticipates claim 1. For example, Verdine discloses **(a)** contacting the target biological molecule (TBM) with individual members of a library of candidate target binding fragments (CTBF's) (e.g., see Verdine, page 5, paragraphs 2-4, especially lines 5 and 16-17 wherein the TBM = DNA equipped with a thiol group and the CTBF's = mixture of peptides with formula CO_2H-Cys-Xaa-NH_2; Please note that the mixture of peptides all contain the requisite -Cys- "disulfide linking group" that is recited in the preamble of claim 1; see also figure 1). Verdine also discloses **(b)** detecting or determining which CTBF's bind to the TBM (e.g., see abstract, "... methods of determining the affinity of a specific binding molecule for a target"). Finally, Verdine also discloses **(c)** selecting CTBF's that bind to the TBM (e.g., see Verdine, page 6, paragraph 2, "Thus, the method described herein is a rational method for the design, selection and production of molecules that bind in a site-specific manner, to desired DNA sequences").

For ***claim 2***, Verdine discloses "quantifying" the binding association of the CTBF's with the TBM by using a reducing gradient (e.g., see page 15, lines 4-5, "The later a dipeptide elutes, the higher its binding affinity for the target DNA sequence [i.e., establishing a mathematical relationship between elution time and binding affinity]"; see also figure 2).

For ***claims 9 and 11***, Verdine discloses linking the selected CTBF's to a second compound (e.g., see page 26, lines 5-8, "Additionally, a second iterative selection can be performed to select a second specific binding molecule to form a heterodimer with the

binding molecule selected in the first iterative cycle. These two specific binding molecules may be cross-linked by conventional methods"; see also page 25, line 34 wherein the CTBF's are bound to a sugar i.e., they are "glycosylated"). Please note that Applicants' claim 9 does not require that the CTBF's be linked to each other (i.e., CTBF-linker-CTBF as in some "SAR by NMR" applications) Claims are to be given their broadest reasonable interpretation consistent with Applicants' specification (e.g., see *In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111. Here, the Examiner's interpretation is consistent with claim 11 where the CTBF's are linked to a second compound instead of each other.

For ***claim 10***, Verdine discloses the use of structurally related analogs (e.g., see page 25, last paragraph wherein "further modifications" are disclosed; see also page 26, paragraphs 1-2).

For ***claims 12-13***, Verdine discloses protein/peptide receptors (e.g., see page 9, paragraph 1, "Examples of targets include ... peptides or proteins (e.g., enzymes, receptors or antibodies)".

For ***claims 16-17***, Verdine discloses CTBF's < 500 Daltons (e.g., see page 5, paragraphs 2-4, especially lines 5 and 16-17 wherein CTBF's = mixture of peptides with formula CO_2H-Cys-Xaa-NH_2, which is << 500 Daltons no matter which amino acid is used for Xaa i.e., di-peptides are ~300 Da).

For ***claim 18***, Verdine discloses a library of a library of tripeptides CO_2H-Cys-Xaa-Xaa-NH_2, which would yield ~ (20 × 20) = 400 library members i.e., there are 20 different amino acids being substituted at each position (e.g., see page 14, line 14).

Claims Rejections – 35 U.S.C. 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-2, 9-13, 16-18 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kim et al. (WO 98/11436) (Date of Patent is **19 March 1998**) (IDS Reference A9) and Cervidil Data Sheet and Morrow et al. (Morrow J. D.; Roberts II, L. J. "Lipid Derived Autacoids: Eicosanoids and Platelet-Activating Factor" The Pharmacological Basis of Therapeutics. Hardman, J. G. and Limbird, L. L. Eds. New York: McGraw-Hill. 2001, page 669) and Lam et al. (Lam, K. S.; Salmon, S. E.; Hersh, E. M.; Hruby, V. J.; Kazmierski, W. M.; Knapp, R. J., "A new type of synthetic peptide library for identifying ligand-binding activity" Nature **1991**, 354, 6348, 82-4).

For ***claims 1***, Kim et al. (see entire document) disclose non-specific affinity enhancement methods (i.e., "tethering") for identifying combinatorial library members (see Kim et al., abstract), which anticipate claim 1. Kim et al. disclose **(a)** contacting the target biological molecule (TBM) with individual members of a library of the candidate target binding fragment (CTBF) (e.g., see page 2, lines 2-5, "The present invention relates to a method of identifying a molecule [i.e., CTBF], present in a collection or library, which binds a target molecule [i.e., TBM]"; see also page 4, middle paragraph disclosing a library of small organic molecules, "the potential ligands present in a collection or library, as well as the target molecule, can be ... small organic molecules"; see also claim 69; see also page 11, paragraph 2 disclosing CTBFs with a disulfide linking group (LG), "As obtained, a target molecule might also include a binding partner (such as a sulfur moiety within a cysteine residue) ... If such a target molecule is used potential ligands [i.e., CTBF] can be modified to include a free sulfhydryl group or a

sulfur that is available for disulfide bond formation through exchange ... Here, non-specific binding of target molecule and potential ligands occurs through formation of a disulfide bond"). Kim et al. disclose **(b)** detecting or determining which CTBF's bind to the TBM (e.g., see Kim et al., page 2, last paragraph, "In one embodiment, the present invention relates to a method of identifying and/or detecting collection or library of potential ligands"). Finally Kim et al. disclose **(c)** selecting CTBF's that bind to the TBM (e.g., see Kim et al., page 3, lines 24-26, "Optionally, the complex of the ligand specifically bound to the target molecule can be separated or removed from the library or collection [i.e., selected]"; see also page 14, lines 12-18 wherein a "selected" ligand is used to make a biased library, "If further ligands are desired (e.g., with greater binding affinity), knowledge of the characteristics of the [selected] ligand can be used to design a biased library of potential ligands ... a region of the ligand identified which appears to be critical for binding is varied based on characterization of the ligand identified").

For ***claim 2***, Kim et al. disclose quantifying the binding association of the CTBF's with the TBM and using this information to design (e.g., see page 14, lines 12-18, "If further ligands are desired (e.g., with greater binding affinity), knowledge of the characteristics of the ligand can be used to design a biased library of potential ligands ... a region of the ligand identified which appears to be critical for binding [i.e., a ligand with a high "quantified" binding affinity] is varied based on characterization of the ligand identified"; see also page 10, paragraph 1 wherein the binding association was "quantified" to be 100 times greater than presently known methods with detection limits "quantified" in the millimolar range).

For ***claim 10***, Kim et al. disclose making analogs with higher binding affinities (e.g., see page 14, lines 12-18, "If further ligands are desired (e.g., with greater binding affinity), knowledge of the characteristics of the ligand can be used to design a biased library of potential ligands... a region of the ligand identified which appears to be critical for binding is varied [i.e., analogs] based on characterization of the ligand identified").

For ***claims 9 and 11***, Kim et al. disclose linking the CTBF's to a second compound like FK506 via a linker (e.g., see figure 2). Please note that Applicants' claim 9 does not require that the CTBF's be linked to each other (i.e., CTBF-linker-CTBF as in some "SAR by NMR" applications) Claims are to be given their broadest reasonable interpretation consistent with Applicants' specification (e.g., see *In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111. Here, the Examiner's interpretation is consistent with claim 11 where the CTBF's are linked to a second compound instead of each other.

For ***claims 12-13***, Kim et al. disclose, for example, hormones (e.g., see page 4, lines 20-28, "As discussed in detail below, the potential ligands present in a collection or library ... can be ... hormones").

For ***claims 16-17***, Kim et al. do not explicitly state that the ligands are "less than about 1000 daltons in size" or "less than 500 daltons in size" (the reference is silent on the issue), but Kim et al. do disclose Applicants' preferred "small organic molecules" and thus must fall within the scope of Applicants' claims (e.g., compare Applicants' claim 1 to Kim et al., claim 11). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or

substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In addition, Kim et al. further disclose the use of "prostaglandins" that inherently possess molecular weights << 500 Da (e.g., see Kim et al., claim 62) as evidenced by the Cervidil data sheet and Morrow et al. Although the reference does not specify a particular prostaglandin and, as a result, the molecular weight of said prostaglandin cannot be determined with certainty, the art recognizes that prostaglandins fall within a class of compounds that contain 20 carbons and thus are limited to ~350 Da in molecular weight as evidenced by the Cervidil data sheet and Morrow et al. (e.g., see Morrow et al., page 669, History section showing prostaglandins belong to the eicosanoid family containing exactly 20 carbons; see also Cervidil data sheet showing a "representative" PGE2 prostaglandin with 20 carbons and a MW = 352.5 Da, which is << 500 or 1,000 Da). When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under

35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) (a case indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. § 102 or obviousness under 35 U.S.C. § 103). See MPEP §§ 2112- 2112.02.

For ***claim 18***, Kim et al. do not explicitly state that the library must comprise "at least 100" different CTBF's (the reference is silent on the issue), but Kim et al. do state that the libraries are produced using the method of Lam et al. (e.g., see Kim et al., Examples 1 and 3). Although Kim et al. do not explicitly state which method steps of Lam et al. were followed and, as a result, the exact number of the library members disclosed by Kim et al. cannot be determined with certainty, there is no indication that the method of Lam et al. was not followed in its entirety, which would produce the same number of library members as in Lam et al. (e.g., see Lam, K. S.; Salmon, S. E.; Hersh, E. M.; Hruby, V. J.; Kazmierski, W. M.; Knapp, R. J., "A new type of synthetic peptide library for identifying ligand-binding activity" Nature **1991**, 354, 6348, 82-4). When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on

inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) (a case indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. § 102 or obviousness under 35 U.S.C. § 103). See MPEP §§ 2112-2112.02.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-2, 4-5, 9-13, 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Verdine (WO 93/141087) (Date of Patent is **July 22, 1993**) and Egorov et al. (Kim, B. B.; Dikova, E. B.; Sheller, U.; Dikov, M. M.; Gavrilova, E. M.; Egorov, A. M. "Evaluation of dissociation constants of antigen-antibody complexes by ELISA" *Journal of Immunological Methods* **1990**, 131(2), 213-222).

For ***claims 1-2, 9-13 and 16-18***, Verdine teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 1-2, 9-13 and 16-18.

The prior art teaching of Verdine differ from the claimed invention as follows:

For ***claims 4-5***, the prior art teachings of Verdine is deficient in that the reference does not recite the use of an ELISA assay for measuring the binding constants.

However, Egorov et al. teach the following limitations that are deficient in Verdine:

For ***claim 4-5***, Egorov et al. (see entire document) teach the usefulness of an ELISA assay for measuring binding constants especially with regard to antigen-antibody interactions (e.g., see Kim et al., abstract).

It would have been obvious to one skilled in the art at the time the invention was made to use the screening methods as taught by Verdine with the ELISA assay as taught by Egorov et al. because Verdine explicitly state that antibody/antigen systems like the one disclosed by Egorov et al. are a preferred embodiment (e.g., see Verdine, page 6, line 29). Furthermore, one of ordinary skill in the art would have been motivated to use the ELISA test to measure receptor/ligand binding affinities as disclosed in Kim et al.

because Egorov et al. explicitly state that the ELISA method can be advantageously used for this purpose (e.g., see Kim et al., page 213, column 1, second paragraph, "A simple and convenient method for determination of K_d values is the enzyme-linked immunosorbent assay (ELISA)"; see also Discussion, "The results described above demonstrate that the solid-phase ELISA provides reproducible and fairly precise estimates of K_d for antigen-antibody complexes ... Its obvious advantages are simplicity and the application of standard ELISA techniques using commercial reagents. Moreover, there is no necessity to label the molecules of the reactants, which can alter their structure") and can be used for the same compounds as disclosed in Kim et al. (i.e., antibody/antigen interactions). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Egorov et al. show successful examples of this technique being applied to antibody/antigen systems like the ones disclosed by Kim et al. (e.g., see Egorov et al., results and conclusion) and also more broadly to other receptor/ligand interactions.

17. Claims 1-2, 4-5, 9-13, 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (WO 98/11436) (Date of Patent is **19 March 1998**) (IDS Reference A9) and Cervidil Data Sheet and Morrow et al. (Morrow J. D.; Roberts II, L. J. "Lipid Derived Autacoids: Eicosanoids and Platelet-Activating Factor" The Pharmacological Basis of Therapeutics. Hardman, J. G. and Limbird, L. L. Eds. New York: McGraw-Hill. 2001, page 669) and Lam et al. (Lam, K. S.; Salmon, S. E.; Hersh, E. M.; Hruby, V. J.; Kazmierski, W. M.; Knapp, R. J., "A new type of synthetic peptide library for identifying ligand-binding activity" *Nature* **1991**, 354,

6348, 82-4) and Egorov et al. (Kim, B. B.; Dikova, E. B.; Sheller, U.; Dikov, M. M.; Gavrilova, E. M.; Egorov, A. M. "Evaluation of dissociation constants of antigen-antibody complexes by ELISA" *Journal of Immunological Methods* **1990**, 131(2), 213-222).

For ***claims 1-2, 9-13 and 16-18***, Kim et al. and the Cervidil Data Sheet and Morrow et al. and Lam et al. teach all the limitations stated in the 35 U.S.C. 102/103 rejection above (incorporated in its entirety herein by reference), which anticipates and/or renders obvious claims 1-2, 9-13 and 16-18.

The prior art teaching of Kim et al. and the Cervidil Data Sheet and Morrow et al. and Lam et al. differ from the claimed invention as follows:

For ***claims 4-5***, the prior art combined teachings of Kim et al. and the Cervidil Data Sheet and Morrow et al. and Lam et al. are deficient in that they do not recite the use of an ELISA assay for measuring the binding constants.

However, Egorov et al. teach the following limitations that are deficient in the combined teachings of Kim et al. and the Cervidil Data Sheet and Morrow et al. and Lam et al.:

For ***claim 4-5***, Egorov et al. (see entire document) teach the usefulness of an ELISA assay for measuring binding constants especially with regard to antigen-antibody interactions (e.g., see Kim et al., abstract).

It would have been obvious to one skilled in the art at the time the invention was made to use screening methods as taught by Kim et al. and the Cervidil Data Sheet and Morrow et al. and Lam et al. with the "ELISA" assay as taught by Egorov et al. because the combined teachings of Kim et al. and the Cervidil Data Sheet and Morrow et al. and

Lam et al. explicitly state that antibody/antigen systems like the one disclosed by Egorov et al. are a preferred embodiment (e.g., see Kim et al., page 4, lines 7-8). Furthermore, one of ordinary skill in the art would have been motivated to use the ELISA test to measure receptor/ligand binding affinities as disclosed in Kim et al. because Egorov et al. explicitly state that the ELISA method can be advantageously used for this purpose (e.g., see Kim et al., page 213, column 1, second paragraph, "A simple and convenient method for determination of K_d values is the enzyme-linked immunosorbent assay (ELISA)"; see also Discussion, "The results described above demonstrate that the solid-phase ELISA provides reproducible and fairly precise estimates of K_d for antigen-antibody complexes ... Its obvious advantages are simplicity and the application of standard ELISA techniques using commercial reagents. Moreover, there is no necessity to label the molecules of the reactants, which can alter their structure") and can be used for the same compounds as disclosed in Kim et al. (i.e., antibody/antigen interactions). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Egorov et al. show successful examples of this technique being applied to antibody/antigen systems like the ones disclosed by Kim et al. (e.g., see Egorov et al., results and conclusion) and also more broadly to other receptor/ligand interactions.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-2, 4-5, 9-13, 16-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of copending Application No. 10/670,607 (Pub. No.: US 2004/0132100 A1) referred to herein as '607. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 4-5, 9-13, 16-18 are generic to all that is recited in claims 1-24 of copending '607. That is, claims 1-24 of copending '607 fall entirely within the scope of claims 1-2, 4-5, 9-13, 16-18 or, in other words, claims 1-2, 4-5, 9-13, 16-18 are anticipated by claims 1-24 of copending '607. For example, claim 1 of '607 falls entirely within the scope of claim 1 of the present application. Specifically, both applications recite **[1]** the same preamble, **[2]** the same first three method steps i.e., 1 (a) - (c) and **[3]** the scope of the structures disclosed for the library members of claim 1 for '607 falls entirely within the scope of claim 1 in the present application because the present application does not limit the scope of the structures (e.g., compare claim 1 in both applications). In addition, dependent

claims 2-18 in both applications are identical and the remaining claims of '60, claims 19-24, only serve to further limit the generic that falls entirely within the scope of claim 1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 20, 2004

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